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Case Report Open Access

Infiltrating Syringomatous Adenoma of the Nipple: A Case Report

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Abstract

We describe a case of a 46-year-old woman who was treated initially for a presumed non-lactational breast abscess.

As symptoms did not subside with conservative management a major duct excision was conducted and histology revealed an infiltrating syringomatous adenoma.

She underwent further surgery to achieve clear margins and the tumour is the largest reported to date.

These are benign, infiltrating lesions and are rare with less than 40 cases reported in the literature.

Patients usually present with a retro-areolar mass and adjacent skin and nipple changes. Radiologically they are difficult to differentiate from breast cancer and diagnosis is largely confirmed through histologic and immunohistochemical analysis.

Treatment is with local excision to achieve clear margins as recurrence rates are high with residual tumour.

Keywords: Syringomatous adenoma; Nipple; Breast abscess

Case Report:

Mrs A, a 46-year-old woman was initially admitted acutely to hospital with a presumed non-lactational breast abscess in the central left breast and commenced on intravenous antibiotics.

She had been assessed nine years previously by a breast surgeon for left nipple discomfort that was thought to be due to duct ectasia. She was offered a duct excision at this time but declined.

She underwent needle aspiration and purulent appearing material was obtained however laboratory analysis did not identify causative bacteria. She experienced clinical improvement and was discharged home.

At subsequent outpatient clinic follow up the area of induration around the left nipple remained along with a small sub-areolar collection on ultrasound, which persisted despite antibiotics and serial aspiration.

Ultrasound did not suggest features concerning for malignancy. As the nipple changes failed to settle the patient was offered left major duct excision. Histology demonstrated appearances suggestive of infiltrating syringomatous adenoma (ISA) of the nipple.

The lesion was 45 × 25 mm, which appears to be the largest case of ISA reported in the literature. As margins were positive, the decision was made for re-excision with complete excision of the left nipple areola complex. Histology confirmed that the residual ISA had been excised with negative margins.

At nearly two years following her surgery, clinical and radiological follow up has been unremarkable. ISA of the nipple are rare, benign tumours that were first described by Rosen in 1983 and are thought to arise from the sweat glands of the nipple areolar complex [1].

They closely resemble duct derived syringomas found elsewhere in the skin, salivary and sweat glands [2]. They are locally infiltrating neoplasms with a high recurrence rate if clear margins are not achieved [3].

It is suggested that the tumour demonstrates no tendency to metastasize however one case report illustrates ISA with evidence of metastases to a local lymph node [2]. To date fewer than 40 cases have been reported in the literature [4].

The small number of reported cases involves patients from 11-76 years of age, with an average age of 40 years [5]. It occurs predominantly in women but cases have been reported in men [6]. Tumour size from previous case reports ranges from 0.5-4 cm [5].

Our case, with a tumour size of 4.5 cm appears to be the largest reported in the literature. It is proposed that patients with a syringomatous adenoma may be at increased risk of developing similar lesions at different sites of the body [5]. The most common presentation of ISA is a mass in the sub-areolar/nipple region, often with surrounding hyperkeratosis of the overlying skin [6].

Nipple discharge occurs infrequently and pain, pruritus and tenderness are occasionally present [6]. Nipple inversion is not usually a prominent feature [3]. Symptoms can be present from months to years [6]. One case report describes ISA presenting as a fungating tumour in an elderly woman who had noticed the changes for several years but refrained from seeking medical attention [4].

Diagnosis is very challenging due to the low number of cases reported, the lack of awareness and the similarities between ISA and tubular carcinoma. In one of the largest case series to date, 7 of 11 cases had initially been incorrectly diagnosed as tubular carcinoma [3]. There are no radiological features classical of ISA and it is not possible to differentiate from carcinoma upon ultrasound or mammography [4].

On mammography ISA predominantly presents as a dense, spiculated mass in the sub-areolar region, however may appear as a poorly defined mass with distal acoustic shadowing [4]. Previous case reports demonstrate a large array of changes on ultrasound examination and in many cases no abnormality is detected. ISA usually appears superficial and closer to the nipple due to its proposed origin from the duct of the dermal sweat glands while tubular carcinoma is often deeper in the breast tissue [5].

It is well documented that fine needle aspiration (FNA) and core biopsy have a limited role in the diagnosis of ISA [4]. Macroscopically they are usually ill-defined, irregular masses with a grey/tan cut surface. Only in rare cases have they presented as well circumscribed lesions. There may be cystic components on the cut surface [7].

The classical microscopic characteristics include two cell layers often resembling a teardrop or comma. It may present as a disorganised assortment of curved, angulated and compressed cordlike tubes and ducts with a clear layer of myoepithelial cells between the epithelial cells and fibrous stroma [2].

It may vary between being primarily glandular or squamous with merging of one element into the other. These areas of squamous epithelium tend to have central lumens lined by "eosinophillic cuticles", very similar to syringomas elsewhere on the body [8,9]. Perineural invasion has been observed in some lesions and was evident in our patient's specimen. Mitotic activity is not usually a feature [8].

Stanford School of Medicine have developed histopathologic diagnostic criteria for ISA:

- Location in dermis and subcutis of nipple or areola.
- Irregular, compressed or comma-shaped tubules infiltrating into smooth muscle bundles or nerves.
- Presence of myoepithelial cells around the tubules.
- Presence of cysts lines by stratified squamous epithelium and filled with keratinous material.
- Absence of mitotic activity and necrosis [10].

Accurate use of immunohistochemistry is a valuable tool in diagnosis of ISA and aids in differentiation from an alternative malignant pathology. Cytokeratin 5/6 (CK5/6) is diffusely positive in myoepithelial cells and heterogeneously positive in epithelial cells (Figure 1).

P63 is also positive in myoepithelial cells and the nuclei of epithelial cells with squamoid differentiation (Figure 2) [4,11].

In the above case many cells were positive for p63 and cytokeratin 5/6 (CK5/6), which supports squamous differentiation and the presence of myoepithelial cells, a feature consistent with ISA.

Smooth muscle myosin (SMM) is reported to be positive in outer myoepithelial cells of the tubules but negative in the luminal epithelia whereas high-molecular-weight cytokeratin (HMW CK) is positive in both myoepithelium and epithelium.

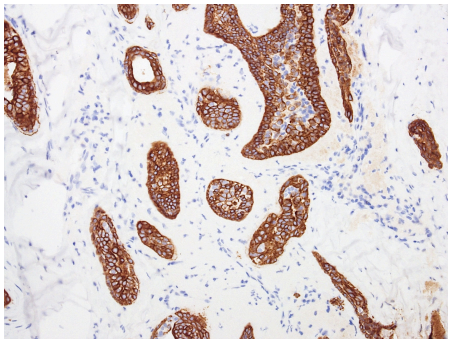

Figure 1: CK5/6

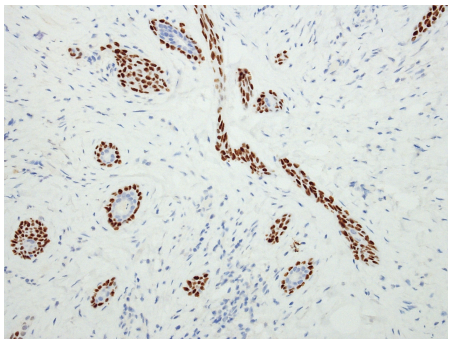

Figure 2: p63.

Estrogen receptor (ER) is weakly positive in the minority of epithelium nuclei and progesterone receptor (PR) is negative. It is very rare for well differentiated breast adenocarcinoma to express p63 or HMW CK [4].

Our laboratory conducted further staining for smooth muscle actin (SMA), S100 and calponin which demonstrated peripheral positivity indicating the presence of myoepithelial cells. It is important to make the differentiation between ISA and tubular carcinoma (TC) as ISA has a more favourable prognosis and generally requires less radical surgical intervention [4].

As both ISA and well-differentiated TC have an infiltrative tendency to invade the surrounding smooth muscle and nerves they can be difficult to differentiate. One of the most important features that helps distinguish between ISA and TC is the presence of two cell layers (epithelial and myoepithelial) in the widespread ducts of ISA in contrast to the single layer of cells in well-differentiated carcinoma.

The presence of squamous differentiation in nearly all ISA is another distinctive feature not observed in well-differentiated adenocarcinoma [8]. As mentioned previously ISA is usually a more superficial lesion. Complete excision with clear margins is the recommended treatment for ISA because of the high risk of recurrence.

One case series demonstrated a 45% recurrence rate however these were due to incomplete excision. Re-excision is appropriate if margins are involved and this usually involves total excision of the nipple-

areolar complex. In patients with clear margins there have been no cases of recurrence with follow up of 1-6 years [12].

Of the small number of patients that have had axillary dissection none have had evidence of tumour within the axillary nodes [6]. Incorrect diagnosis of ISA may result in overtreatment with mastectomy when wide local excision is appropriate. There is currently no clear guidance as to what margins are considered satisfactory for complete excision and adjuvant therapy is not recommended.

There are currently no clear guidelines as to follow up. With high recurrence rates in incomplete excision, limited knowledge of the disease process and diagnostic challenges, long term follow up is recommended by our institution. This paper adds to the medical literature, a rare case of an ISA of the nipple. To our knowledge this is the largest reported ISA.

Even though it is a rare and benign condition, it is an important diagnosis as it closely mimics more malignant pathology and treatment is vastly different.

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